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Periodontitis Prevalence and Severity in Indonesians With Type 2 Diabetes

Hendri Susanto,* Willem Nesse,† Pieter U. Dijkstra,‡ Dewi Agustina,* Arjan Vissink,† and Frank Abbas§||

Background: The prevalence of diabetes mellitus type 2 (DM2) in Indonesia is high and still rising. Periodontitis is associated with DM2. No study has investigated this association in Indonesia, nor has any study investigated this association using a variety of methods to operationalize periodontitis. The present study compares prevalence and severity of periodontitis in patients with DM2 to healthy controls, using different methods to operationalize periodontitis.

Methods: A total of 78 subjects with DM2 and 65 healthy control subjects underwent a full-mouth periodontal screening assessing probing depth, gingival recession, plaque index, and bleeding on probing. Using these measurements, the prevalence and severity of periodontitis was operationalized in various ways. Differences in the prevalence and severity of periodontitis between subjects with DM2 and healthy subjects were analyzed using univariate analyses. In regression analyses, the prevalence and severity of periodontitis were predicted on the basis of DM2 presence, controlling for confounders and effect modification.

Results: Prevalence of periodontitis was significantly higher in subjects with DM2 compared to healthy subjects, showing odds ratios of 5.0 and 6.1. Likewise, periodontitis severity was significantly higher in subjects with DM2.

Conclusion: Indonesian subjects with DM2 had more prevalent and more severe periodontitis than healthy Indonesian subjects, independent of confounding factors or the methods used to operationalize periodontitis. *J Periodontol* 2011; 82:550-557.

KEY WORDS

Diabetes mellitus; periodontal inflamed surface area; periodontitis.

Diabetes mellitus (DM) is a chronic disease characterized by dysregulation of carbohydrate, protein, and lipid metabolism. An elevation of blood glucose level (hyperglycemia) is the primary feature of DM and results from a defect in insulin secretion by pancreatic β cells, a decrease in insulin sensitivity, or a combination of both. The most common form of DM is DM type 2 (DM2), which accounts for 85% of all diabetes patients.¹ The estimated worldwide prevalence of DM is 220.5 million, or 2.8% of the world's population. DM currently is the twelfth leading cause of death in the world. The prevalence is estimated to rise up to 4.4%, putting DM in the top 10 leading causes of death by 2030.^{2,3} With the increasing prevalence of DM, this already vast and worldwide epidemic will increasingly pose serious problems to public health. These problems mostly arise from the complications associated with DM, such as myocardial infarction, cerebrovascular disease, retinopathy, nephropathy, and neuropathy.⁴

Periodontitis is more prevalent and severe among patients with DM2 than among healthy controls.⁵⁻⁷ Thus, DM2 may initiate or deteriorate periodontitis. However, the reverse could also be true: periodontitis may initiate or deteriorate DM2. The strongest support for this comes from studies showing that treatment of periodontitis improves glycemic control in DM2 patients.⁸⁻¹³ Thus, there is an association between DM2

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and periodontitis that seems to be bilaterally causal in nature (i.e., one causes or deteriorates the other and vice versa).

The strength of associations between periodontitis; and DM2 seems to differ geographically. Studies performed among different ethnic groups show different associations between periodontitis and DM2.^{5,14-17} These differences in the strength of associations may, apart from differences in study design and data analysis, be based on genetic, dietary, cultural, and other differences among ethnic groups.¹⁸ Therefore, findings among one ethnic population cannot automatically be generalized to another ethnic population.

South East Asia hosts approximately 10% of the world's current population. With 240 million inhabitants, Indonesia is the fourth most populous country in the world. The prevalence of DM in South East Asia is 5.3%.¹⁹ In Indonesia, the prevalence of DM in 2008 was 5.7%,²⁰ putting Indonesia in the top 10 countries with the most DM patients in the world. By the year 2030, the estimated number of patients with DM in Indonesia will be >20 million ($\approx 10\%$ of the population).² With this high and rising prevalence of DM2 in Indonesia, periodontitis prevalence and severity may also rise. Only three studies report on the association between periodontitis and DM2 in South East Asia: Thailand,²¹ Singapore,²² and Indonesia.²³ Unfortunately, in the latter study, the way in which periodontitis was measured and defined is unclear. This study did not make a distinction between patients with DM1 and DM2, leaving many questions unanswered.

Also remaining unanswered is the influence of using a particular method to operationalize periodontitis on the strength of an association between periodontitis and DM2. The use of different methods to operationalize periodontitis prevalence and severity may influence not only the strength of the associations between a given disease and periodontitis, but may even influence whether an association is observed at all. For example, in research linking periodontitis to preterm low birth weight, 13 different methods have been used to operationalize periodontitis. Depending on the method used, either an association^{24,25} or no association²⁶ between periodontitis and preterm low birth weight was observed. The same may be true for periodontitis and DM2.

The present study assesses prevalence and severity of periodontitis among DM2 patients in Indonesia, using multiple, commonly used methods to operationalize both periodontitis prevalence and severity.

MATERIALS AND METHODS

Subjects

DM2 patients were recruited at three different sites in Yogyakarta, Indonesia: 1) Internal Medicine Depart-

ment of the Dr. Sardjito Hospital; 2) Prof. Soedomo Oral and Dental Hospital, Faculty of Dentistry, Gadjah Mada University; and 3) Diabetes Center of Jogjakarta International Hospital. DM2 patients were diagnosed according to World Health Organization criteria: fasting blood glucose level ≥ 126 mg/dl or a postprandial blood glucose level ≥ 200 mg/dl.²⁷ Healthy controls were recruited in Prof. Soedomo Oral and Dental Hospital Gadjah Mada University. Inclusion criteria for all subjects were ≥ 18 years of age and with ≥ 8 teeth. This study was approved by the Ethical Committee for Research of the Medical Faculty of Gadjah Mada University, and was conducted from July 2008 to February 2009.

To assess whether periodontitis prevalence and severity differed between DM2 patients and healthy controls, 78 DM2 patients (35 males and 43 females) and 65 healthy controls (22 males and 43 females), who gave oral informed consent, underwent a full-mouth periodontal examination. Full-mouth periodontal probing depth (PD), gingival recession, plaque score, and bleeding on probing (BOP) measurements were performed on all teeth, six sites per tooth. All permanent fully erupted teeth were examined with a manual periodontal color-coded standard probe.[¶] Measurements were made in millimeters and were rounded to the nearest whole millimeter. Clinical attachment loss (AL) was defined as the distance from the cemento-enamel junction to the bottom of the pocket/sulcus, and calculated as the mathematical sum of the PD and gingival recession measurements.²⁸ BOP was recorded as either present or absent within 30 seconds after probing at six sites per tooth. The number of missing teeth was also recorded. Plaque was defined as being present or absent at six points on each tooth.²⁹

Periodontitis prevalence, extent, and severity were operationalized using a variety of methods, all of which are currently used to study the association between periodontitis and other diseases. All methods were calculated using conventional clinical measurements obtained during the periodontal examination. Periodontitis prevalence was operationalized by using two diagnostic threshold values: having one site with PD ≥ 4 mm and clinical AL ≥ 3 mm,²⁶ and having one site with PD ≥ 5 mm and clinical AL ≥ 2 mm.³⁰ The following methods to operationalize periodontitis extent and severity were calculated using an online spreadsheet:[#] the number of sites with PD ≥ 4 , ≥ 5 , and ≥ 6 mm; the numbers of sites with clinical AL ≥ 3 , ≥ 4 , ≥ 5 , and ≥ 6 mm; mean PD; mean clinical AL; and the percentage of sites with BOP.²⁶

¶ DENTSPLY, London, UK.

Microsoft Excel 2003 spreadsheet for Windows, Microsoft, Redmond, WA.

Table 1.**Characteristics of Healthy Controls and Subjects With DM2 and Potential Determinants of Periodontitis Severity**

Patient Characteristics	Controls (n = 65)	DM2 (n = 78)	Difference (95% confidence interval)	P Value
Age: mean (SD) years	50.5 (10.6)	56.7 (9.4)	6.2 (2.8 to 9.5)	<0.00*
Sex: n (%)				0.180†
Male	22 (34)	35 (45)		
Female	43 (66)	43 (55)		
Smoking: n (%)	10 (15)	14 (18)		0.683†
Java origin: n (%)	60 (92)	73 (94)		0.765†
Education: n (%)				0.762†
Low	17 (26)	18 (23)		
Middle	26 (40)	29 (37)		
High	22 (34)	31 (40)		
BMI (SD) (kg/m ²)	24.6 (3.9)	25.1 (3.8)		0.460‡
Number of teeth (SD) (n)	24.5 (5.5)	22.9 (6.1)		0.112‡
Plaque score (SD) (%)	92.5 (9.2)	90.8 (7.6)		0.211‡
Medical conditions: n (%)‡				
Hypertension	12 (18)	26 (33)	15% (0.3 to 29)	<0.05*§
Gastritis	4 (6)	10 (13)		0.182§
Anemia	2 (3)	0 (0)		0.119§
Angina Pectoris	0 (0)	3 (4)		0.110§

Education: low, elementary and junior school; middle, high school; high, university.

* Statistically significant difference ($P \leq 0.05$) between DM2 and controls.† χ^2 test.‡ Independent samples t test.

§ Only diseases with a prevalence of at least 1% (i.e., two patients) were analyzed.

Additionally, two recently introduced measures of periodontitis severity, the periodontal epithelial surface area (PESA) and the periodontal inflamed surface area (PISA),³¹ were both calculated using the downloadable spreadsheet.** PESA reflects the surface area of all pocket epithelium in square millimeters, whereas PISA reflects the surface area of bleeding pocket epithelium in square millimeters. PESA and PISA are calculated using conventional clinical AL, gingival recession, and BOP measurements. PISA quantifies the amount of inflamed periodontal tissue and it is suggested that PISA thereby quantifies the inflammatory burden posed by periodontitis.

All participants completed a validated general health assessment questionnaire³²⁻³⁴ to identify other medical conditions that might be a risk factor for periodontitis. The original questionnaire was translated from English into Indonesian; a reverse translation to English was made to check for potential differences. No substantial differences were found. Additionally, ethnicity,³⁵ body mass index (BMI),³⁶ dental plaque, age, sex, smoking (pack-years), and socioeconomic

status (SES) (operationalized using level of education) were recorded for each participant (Table 1), because these are potential determinants of periodontitis.³⁷

To ensure that healthy controls were not undiagnosed patients with diabetes, all participants underwent venipuncture. Blood glucose and glycated hemoglobin (HbA_{1c}) were determined for both DM2 patients and healthy controls. Controls with a blood HbA_{1c} level of $\geq 6.5\%$ were excluded from the analysis, to exclude latent DM2 status.

Statistical Analyses

Differences in periodontitis prevalence, extent, and severity between DM2 patients and healthy subjects were analyzed first using univariate analyses (independent sample t test or χ^2 test as appropriate). Likewise, differences in potential predictors of periodontitis (age, sex, BMI, SES, smoking, plaque score, number of teeth, ethnicity, and other medical conditions) between DM2 patients and healthy controls were tested for significance using univariate analyses. In case

** Microsoft Excel 2003 spreadsheet for Windows, Microsoft.

Table 2.**Differences in Periodontitis Prevalence Between Healthy Controls and Subjects With DM2**

Periodontitis Prevalence	Controls (n = 65)	DM2 (n = 78)	Difference (95% confidence interval)	OR (95% confidence interval)	P Value
PD4&AL3 (yes)	46 (71%)	72 (92%)	21% (9% to 32%)	5 (1.8 to 13.3)	0.001*†
PD5&AL2 (yes)	20 (31%)	57 (73%)	42% (26% to 55%)	6.1 (2.9 to 12.6)	<0.001*†

OR: Odds ratios were calculated using binary logistic regression analyses controlling for confounders.

PD4&AL3 = participants with one site exhibiting both PD 4 mm and clinical AL 3 mm; PD5&AL2 = participants with one site exhibiting both PD 5 mm and clinical AL 2 mm.

* Statistically significant difference ($P \leq 0.05$) between DM2 and controls.

† χ^2 test.

Table 3.**Differences in Periodontitis Severity Between Healthy Controls and Subjects With DM2**

Periodontitis Severity	Controls (n = 65) Mean (SD)	DM2 (n = 78) Mean (SD)	Difference (95% confidence interval)	P Value
PESA (mm ²)	863 (259.4)	1,190.5 (1161.5)	327.5 (58.3 to 596.6)	0.018*
PISA (mm ²)	154.1 (192.1)	429.4 (964.9)	275.3 (52.9 to 497.6)	0.016*
Number of sites with				
Clinical AL ≥ 3 mm	35.8 (23.1)	63.5 (29.9)	27.6 (18.8 to 36.4)	<0.001*
Clinical AL ≥ 4 mm	12.3 (15.1)	37.1 (27.2)	24.8 (17.7 to 31.9)	<0.001*
Clinical AL ≥ 5 mm	5.9 (10.2)	22.9 (21.4)	16.9 (11.5 to 22.4)	<0.001*
Clinical AL ≥ 6 mm	3.1 (7.3)	13.7 (16.2)	10.6 (6.6 to 14.7)	<0.001*
PD ≥ 4 mm	4.5 (7.9)	16.6 (21.2)	12.1 (6.9 to 17.3)	<0.001*
PD ≥ 5 mm	1.4 (3.7)	7.7 (12.5)	6.3 (3.4 to 9.2)	<0.001*
PD ≥ 6 mm	0.8 (2.3)	4.5 (9.3)	3.7 (1.5 to 5.9)	0.001*
BOP (%)	14.2 (13.3)	24.9 (16.1)	10.7 (5.8 to 15.5)	<0.001*
Clinical AL mean (mm)	2.2 (0.9)	3.1 (1.3)	0.9 (0.5 to 1.3)	<0.001*
PD mean (mm)	1.8 (0.4)	2.2 (0.6)	0.4 (0.2 to 0.5)	<0.001*

* Statistically significant difference ($P \leq 0.05$) between DM2 and controls.

periodontitis prevalence, extent, and severity and any of the potential predictors of periodontitis differed significantly between DM2 patients and healthy controls, the predictors of periodontitis other than DM2 might act as confounders or effect modifiers.

Because periodontitis severity was operationalized as several interval variables (PISA, or number of sites with PD ≥ 4 mm), linear regression analyses (Table 4) (backward stepwise) were performed to predict extent and severity of periodontitis on the basis of DM2 presence and the other potential predictors (age, sex, BMI, SES, smoking, plaque score, number of teeth, ethnicity, and other medical conditions). To facilitate clinical interpretation of presented analyses, age was centered to its mean (53.86). Because periodontitis prevalence was operationalized as two dichotomous variables, logistic regression analyses were performed in a similar way. Odds ratios

and 95% confidence intervals were calculated using these logistic regression analyses. Interaction among different predictors of periodontitis was explored. Statistics were calculated using a software program.††

RESULTS

Of the original 76 healthy controls, 11 subjects were excluded because of HbA_{1c} levels $>6.5\%$, leaving 65 healthy controls and 78 DM2 patients (Table 1). The prevalence of periodontitis in DM2 subjects was significantly higher than healthy controls, regardless of the definition used (Table 2). The extent and severity of periodontitis was also significantly higher in participants with DM2 compared to controls, again independent of the method used to operationalize periodontitis severity (Table 3).

†† SPSS 16.0, IBM, Chicago, IL.

Table 4.

DM2 and Age as Statistical Predictors of Periodontitis Extent and Severity: Results of Multiple Linear Regression Analyses With Periodontitis Operationalized According to Commonly Used Definitions

Dependent Variable and Model Predictors	β Unstandardized	β Standardized	P Value of β^*	R^2	95% Confidence Interval of β
PESA				0.03	
DM2	327.49	0.18	<0.05		36.65 to 618.33
Constant	863.04		<0.001		648.25 to 1077.84
PISA				0.04	
DM2	275.29	0.19	<0.05		34.69 to 515.89
Constant	154.06		0.089		-23.63 to 331.76
BOP %				0.11	
DM2	10.65	0.34	<0.001		5.71 to 15.60
Constant	14.23		<0.001		10.58 to 17.89
PD ≥ 4 mm [†]				0.12	
DM2	12.10	0.34	<0.001		6.60 to 17.60
Constant	4.92		<0.05		0.43 to 8.56
PD ≥ 5 mm [†]				0.10	
DM2	6.30	0.31	<0.001		3.13 to 9.47
Constant	1.35		0.254		-0.98 to 3.69
PD ≥ 6 mm [†]				0.07	
DM2	3.70	0.26	0.002		1.36 to 6.03
Constant	0.75		0.388		-0.97 to 2.47
PD mean				0.11	
DM2	0.37	0.33	<0.001		0.19 to 0.54
Constant	1.83		<0.001		1.70 to 1.96
Clinical AL ≥ 3 mm [†]				0.24	
DM2	24.25	0.40	<0.001		14.99 to 33.49
Age centered	0.54	0.19	0.017		0.10 to 0.98
Constant	37.7		<0.001		31.0 to 44.4
Clinical AL ≥ 4 mm [†]				0.29	
DM2	20.85	0.41	<0.001		13.31 to 28.40
Age centered	0.64	0.26	0.001		0.28 to 1.00
Constant	14.5		<0.001		9.0 to 19.9
Clinical AL ≥ 5 mm [†]				0.25	
DM2	14.12	0.37	<0.001		8.31 to 19.94
Age centered	0.46	0.25	0.002		0.18 to 0.74
Constant	7.5		0.001		3.26 to 11.68
Clinical AL ≥ 6 mm [†]				0.19	
DM2	8.82	0.32	<0.001		4.42 to 13.22
Age centered	0.29	0.22	0.008		0.08 to 0.50
Constant	4.03		0.013		0.85 to 7.22
Clinical AL mean [†]				0.21	
DM2	0.71	0.29	<0.001		0.33 to 1.09
Age centered	0.03	0.27	0.001		0.01 to 0.05
Constant	2.27		<0.001		2.00 to 2.54

Age-centered = age minus mean age; constant = sites with PD ≥ 4 mm that are not dependent on DM2 presence or increasing age; β = unstandardized coefficient; number of sites with clinical AL = clinical attachment loss ≥ 3 , ≥ 4 , ≥ 5 , and ≥ 6 mm; number of sites with PD = probing depth ≥ 4 , ≥ 5 , and ≥ 6 mm.

* P value of ≤ 0.05 was considered statistically significant.

† Number of sites.

Age and hypertension were the only potential predictors of periodontitis prevalence and severity that differed significantly between DM2 and healthy subjects in the univariate analysis (Table 1). In the multiple linear regression analyses, controlling for age and hypertension as potential confounders, DM2 remained a significant predictor of all measures of periodontitis severity (Table 4). Age was an additional predictor of periodontitis severity, together with DM2, whenever periodontitis severity was operationalized using AL. Age did not modify the effect of DM2 on periodontitis severity. Hypertension was not a predictor of periodontitis prevalence or severity.

DISCUSSION

This study reveals that Indonesian subjects with DM2 had significantly increased prevalence, extent, and severity of periodontitis compared to healthy Indonesian subjects. Moreover, these increases were independent of the methods used to operationalize periodontitis. Furthermore, these increases seemed to be independent of confounding factors, i.e., age, sex, smoking, BMI, ethnicity, SES, and other medical conditions.

Age was an additional predictor of all methods that used clinical AL to operationalize periodontitis severity. This could have been expected because clinical AL reflects the accumulation of damage sustained by the periodontium over time. In other words, with increasing age, clinical AL increases. Nevertheless, DM2 remained a significant predictor of every method used to operationalize periodontitis prevalence and severity.

Before the study we did not perform a formal sample-size calculation, although this study is the second on periodontitis and DM2 in Indonesia. It is not clear how periodontitis was measured and defined in the first study, and no distinction was made among patients with DM1 and DM2.²³ In a post hoc power analysis it seemed that we had a power of 0.92 to find a difference in prevalence of periodontitis of 21% between controls ($n = 65$; prevalence = 71%) and DM2 patients ($n = 78$; prevalence = 91%). A sample of 50 DM2 patients and 50 controls would have been enough to detect this difference (power, 0.80).

A limitation of this study is that we did not use a population-based sampling scheme to select DM2 patients. However, Indonesian patients with DM2 regularly visit hospitals to make use of the laboratory facilities. Thus, selection of DM2 patients at the two internal medicine hospitals does not mean a subset of patients with more severe DM2 patients was selected. Rather, these subjects may be thought to represent a sample of diagnosed and treated Indonesian patients with DM2. However, true DM2-associated

increased periodontitis risk may be underestimated, because a substantial portion of patients with DM2 often goes undiagnosed. Likely, these patients have worse blood sugar control and consequently worse periodontal status. On the other hand, the DM2 patients that were recruited from a dental hospital may have visited this hospital for periodontitis, overestimating DM2-associated periodontitis prevalence in this subgroup. Likewise, because controls were all selected from the same dental hospital, the prevalence of periodontitis in controls may also have been overestimated. Because the prevalence in both groups might be overestimated, the overall effect on calculated DM2-associated periodontitis risk may have been small. Finally, selection of healthy controls at a dental hospital may not be representative of the general Indonesian population without DM2. Thus, although some threats to the generalizability of our results remain, the increased DM2-associated periodontitis risk does seem to have sufficient generalizability and might sooner have been underestimated rather than overestimated.

The finding that DM2 subjects have an increased prevalence and severity of periodontitis is in accordance with other studies.^{30,38,39} A major achievement of the present study is that a large variety of methods to operationalize periodontitis prevalence and severity has been applied, and that the conclusions that could be drawn from the results were irrespective of the measures used. This indicates that this association is robust. Because the prevalence of DM2 in Indonesia²⁰ and South East Asia¹⁹ is already high and is predicted to rise further, the prevalence and severity of periodontitis may also rise. Because of the vast number of people living in Indonesia and South East Asia and the proposed bilateral association between DM2 and periodontitis, this will increasingly pose serious problems to public health.

Two main mechanisms are thought to underlie the proposed bilateral association between DM2 and periodontitis. One underlying mechanism is that DM2 may alter local immune responses within periodontal tissue. DM2 may result in small vessel damage within the periodontium, resulting in poor nutrient delivery, decreased oxygen diffusion, and decreased elimination of metabolic waste products.⁴⁰ Furthermore, hyperglycemia alters collagen metabolism, which predisposes to impaired wound healing. In general, hyperglycemia results in the formation of proteins known as advanced glycation end products (AGEs). AGEs may be associated with a state of enhanced oxidative stress, thereby accelerating tissue injury. AGEs also function as a chemotactic for monocytes, thereby magnifying the inflammatory response, delaying wound healing and tissue repair

and inducing connective-tissue damage and bone resorption. Finally, hyperglycemia and the imbalance in lipid metabolism impair neutrophil and monocyte functioning.⁴¹⁻⁴⁴ All of these factors may contribute to DM2 predisposing to periodontitis.

The second underlying mechanism of the association between DM2 and periodontitis is that periodontitis may play a role in initiating or exacerbating DM2.^{7,43,45} Periodontitis poses an inflammatory burden consisting of increased serum levels of inflammatory mediators, such as C-reactive protein and interleukin-6.⁴⁶ This inflammatory burden in turn leads to deteriorating blood glucose control in DM2 patients.⁴³ The higher the amount of inflamed periodontal tissue, the higher the inflammatory burden, and the poorer blood glucose control in DM2 patients may be thought to be.

PISA quantifies the amount of inflamed periodontal tissue (representing it as the surface area of inflamed periodontal epithelium in square millimeters), and it is suggested that PISA thereby quantifies the inflammatory burden posed by periodontitis.³¹ It was shown that there is indeed a dose relationship between PISA and HbA_{1c} in patients with DM2 in the Dutch Caribbean.⁴⁷ Likewise, the finding of a significantly higher PISA among DM2 subjects in the present study may mean that periodontitis is a risk factor for poor glucose control. Treating periodontitis might improve blood glucose control,⁸⁻¹³ and prevention and treatment of periodontitis in patients with DM2 might contribute to better general health in patients with DM2.^{48,49}

CONCLUSIONS

This study shows that periodontitis prevalence is significantly higher in a group of Indonesian patients with DM2 compared to a group of healthy Indonesians. Furthermore, Indonesian subjects with DM2 have more extended and more severe periodontitis than healthy Indonesian subjects. Given the already high and increasing prevalence of DM2 in Indonesia, patients with DM2 should be screened for periodontitis and preventive oral health care should become part of the regular care provided to Indonesian patients with DM2. Given the proposed bilateral association between DM2 and periodontitis, such care may contribute to better oral and overall health.

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